EXHIBIT P

AMERICAN JOURNAL OF INDUSTRIAL MEDICINE 51:258–268 (2008)

Occupational Risk Factors for Non-Hodgkin's Lymphoma: A Population-Based Case–Control Study in Northern Germany

David B. Richardson,[1]* Claudia Terschüren,[2] and Wolfgang Hoffmann[2]

Objectives *To identify occupational factors associated with non-Hodgkin's lymphoma (NHL).*
Methods *A population-based case–control study was conducted in which incident cases of high-malignancy NHL (NHL_{high}), low-malignancy NHL (NHL_{low}), and chronic lymphocytic leukemia (CLL) were ascertained during the period 1986–1998 among men and women aged 15–75 years residing in six German counties; controls were drawn from population registries. Occupational histories were collected and agent-specific exposures were estimated via a job-exposure-matrix. Odds ratios were estimated by conditional logistic regression.*
Results *A total of 858 cases were included in these analyses. Agricultural workers [odds ratio (OR) = 2.67, 95% confidence interval (CI): 0.99, 7.21) and farmers (OR = 1.98, 95% CI: 0.98, 3.98] had elevated risk of NHL_{high}. Risk of NHL_{low} was elevated among agricultural workers (OR = 2.46, 95% CI: 1.17, 5.16), and among blacksmiths, toolmakers, and machine tool operators (OR = 3.12, 95% CI: 1.31, 7.47). Workers in sales and construction had elevated risks of NHL_{high} and NHL_{low}. Exposure to arsenic compounds, chlorophenols, diesel fuel, herbicides, nitrites/nitrates/nitrosamines, and organic dusts were associated with NHL_{high} and NHL_{low}, while exhibiting little association with CLL. A positive monotonic trend in NHL_{low} risk across tertiles of cumulative diesel fuel exposure was observed [P-value for test of linear trend (P) = 0.03].*
Conclusions *These findings provide insights into several potential occupational risk factors for NHL and suggest some specific occupational agents for further investigation.*
Am. J. Ind. Med. 51:258–268, 2008. *© 2008 Wiley-Liss, Inc.*

KEY WORDS: case–control study; non-Hodgkin's lymphoma; occupation; Germany

INTRODUCTION

Non-Hodgkin's lymphomas (NHL) account for about 4% of cancer diagnoses and 3% of cancer deaths in the United States [Jemal et al., 2006]. Over the last three decades, the incidence of NHL has increased in the United States and most European countries with NHL mortality rates nearly doubling in the US since the 1970s [Hartge et al., 2006]. Such a marked change over time in NHL rates is suggestive of an important role of environmental or occupational exposures in NHL etiology [Pearce and Bethwaite, 1992]. Diet and physical activity are not strongly associated with NHL risk, and cigarette smoking has been found to have, at most, a

[1]Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina
[2]Institute for Community Medicine, Section Health Care Epidemiology and Community Health, Ernst-Moritz-Arndt-University Greifswald, Greifswald, Germany
Contract grant sponsor: Alfried Krupp von Bohlen und Halbach-Stiftung; Contract grant sponsor: Ministry of Environment, Nature Protection and Agriculture, Schleswig-Holstein; Contract grant sponsor: Ministry of Social Affairs, Women, Family and Health, Lower Saxony.
*Correspondence to: David B. Richardson, Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599.
E-mail: david.richardson@unc.edu

Accepted 11 October 2007
DOI 10.1002/ajim.20552. Published online in Wiley InterScience (www.interscience.wiley.com)

modest effect on the incidence of NHL [Zahm et al., 1997; Schroeder et al., 2002; Morton et al., 2005]. There is a strong association between NHL risk and acquired immunodeficiencies (including AIDS), although factors associated with immunodeficiencies do not appear to explain the temporal trends in NHL rates in the US and Europe [Hartge et al., 2006].

Studies of associations between NHL risk and employment in specific occupations or industries provide a starting point for etiologic research on occupational risk factors for NHL. Prior studies have suggested elevated NHL risk among workers employed in a number of occupations including farming, forestry, pesticide application, and metal working trades [Zheng et al., 2002; Dryver et al., 2004; Hartge et al., 2006]. The present investigation aimed to evaluate the association between occupational exposures and NHL risk in a large population-based case–control study in Germany, utilizing occupational titles as well as exposure estimates derived from a job-exposure-matrix (JEM).

METHODS

Case and Control Recruitment

Cases were defined as newly-diagnosed cases of NHL that occurred between 1986 and 1998 among men and women who were German nationals 15–75 years of age residing in the counties of Herzogtum Lauenburg, Steinburg, Stormarn, Pinneberg, Harburg, and Lüneburg in the German Federal States of Schleswig-Holstein and Lower Saxony, excluding the urban area of Hamburg. Cases of chronic lymphocytic leukemia (CLL) were also included. Ascertainment of cases was mostly retrospective, with field work for case ascertainment beginning in February, 1997. Cases were ascertained from all hospitals in the study counties, all hospitals in neighboring counties, two university hematologic clinics, all general practitioners specialized in internal medicine, oncology, general medicine, and pediatrics, as well as private practices specialized in outpatient care of cancer patients in the study area, all pathology and cytology institutes, and the public health offices of the study counties (which serve as death certificate registries). Cases were actively ascertained on-site by comprehensive screening of all patients' files and other primary patient documentation (i.e., pathology reports, radiation therapy files) in all institutions. Relevant study variables were abstracted to standardized forms by trained study staff. Each patient was contacted directly by their treating physician for recruitment into the study.

The diagnostic category of NHL encompasses a heterogeneous group of malignant lymphatic diseases. NHL cases were divided into subgroups, following the revised Kiel classification, as high malignancy NHL (NHL_{high}) and low malignancy NHL (NHL_{low}) [Lennert and Feller, 1992]. We used the full text diagnoses sometimes considering additional information (e.g., from histopathologic reports). Twenty two cases of NHL could not be classified as low or high malignancy due to insufficient detail in the available records. We excluded those cases from our analyses. CLL is regarded a non-Hodgkin's lymphoma of low malignancy according to all modern classifications. To allow for comparison with previous reports in the literature, where traditionally CLL has been grouped with the leukemias, we include CLL as a separate category in these analyses.

Controls were ascertained from population registries for the study counties; registration of residents is mandatory in Germany. Controls were individually matched to each case on sex, year of birth (± 2 years), and region (broadly classified as western vs. eastern study regions). At least two controls were sampled for each case. Controls were required to be free of diagnosed leukemia or lymphoma at the end of the study period.

Data Collection and Exposure Assessment

In-person interviews were conducted by trained interviewers who used a computer-assisted survey tool. The questionnaire asked about education, smoking history, lifelong residential history, exposure to diagnostic or therapeutic X-rays, and consumption of locally produced foods. The questionnaire also elicited a detailed occupational history. A person was permitted to report that they held multiple jobs at one time; each job was recorded as well as the estimated number of hours worked in each job. Because of refusals, 30% of the ascertained cases did not complete the interview. Controls were interviewed using the same protocol used for cases. Among the controls, 55% of those initially contacted and eligible for inclusion in the study completed the interview. For more detailed response statistics please refer to the accompanying paper.

Job titles were classified according to the International Standard Classification of Occupations (ISCO) of the International Labor Office, revised edition, 1968 [International Labor Organization, 1969]; and, branches of industry were coded according to the first revision of the Statistical Classification of Economic Activities in the European Community (NACE) [Eurostat, 1990]. These classifications were based upon five and four digit codes, respectively. For descriptive analyses workers were classified into the longest held occupation classified into major (one-digit codes) and minor (two-digit codes) ISCO categories.

Estimates of exposure to 50 chemical, physical, and biological agents were derived by means of a JEM [Pannett et al., 1985]. Information was used on each occupation and industry held by a person up to the date of selection as a case or control. Separate exposure ratings were provided for

employment in calendar periods prior to, and subsequent to, 1950. Exposures were rated on two scales. ''Probability'' of exposure represented the likelihood of exposure based upon knowledge of the materials and processes associated with a given occupation and industry group and was classified as low, medium, or high (and assigned scores of 0, 1, and 3, respectively). ''Intensity'' of exposure represented the estimated exposure rate and also was assigned scores of 0, 1, and 3. A quantitative exposure score for each agent was calculated as the product of the assigned probability score, intensity score, and the total number of hours employed in a given job. Cumulative exposure to the agent was defined as the sum of these exposure scores over a person's occupational history.

Smoking histories were assessed by a series of questions that asked whether the person ever smoked cigarettes, cigars, or a pipe. For each type of tobacco smoked, the age or year started, the amount smoked per day, and the age or year stopped were recorded for every change in habit. A composite index of socioeconomic status was created based upon information on household income, household size, and education. This index was used in descriptive analyses but not adjusted for in analyses of occupational exposure-disease associations due to its role as a potential surrogate for exposure.

Statistical Analysis

Conditional logistic regression models were fitted to these data via the SAS (version 9.1) software package in order to obtain estimated odds ratios and associated confidence intervals [SAS Institute Inc., 2004]. All models were conditioned on the factors defining the matched sets and were adjusted for a three-level indicator of smoking status (never smoker vs. ex-smoker vs. current smoker). Odds ratios were calculated for workers classified by longest-held occupation (according to two-digit ISCO codes); and, odds ratios were calculated for ever versus never employed in jobs judged to involve potential exposure to 50 occupational agents. Analyses of the association between potential exposure to each of the 50 occupational agents and disease risk were conducted one occupational agent at a time, as opposed to deriving effect estimates that simultaneously adjusted for potential exposures to all other assessed agents. Occupational exposure classifications were lagged by discounting exposures accrued in the 2 years prior to case diagnosis or the date on which a control attained the age of its matched case. Trends in disease risk were examined by fitting a model with categorical terms for categories of cumulative exposure to the specified agent, as well as by fitting a model with a continuous term for cumulative exposure to the agent. For analyses in which cumulative exposure was categorized, exposure categories were based upon the distribution of exposure among all exposed controls, with tertiles used as cutoff points; people never exposed to the agent constituted the reference group. For analyses in which a continuous term was fitted for cumulative exposure, we report a *P*-value as a test for linear trend in the log-odds of disease with increasing exposure; this *P*-value is based upon a Wald Chi-square test statistic for the null hypothesis (i.e., the beta coefficient for the linear term for cumulative exposure is equal to zero). Separate analyses were conducted for NHL_{high}, NHL_{low}, and CLL.

The study design was approved by the ethics committee and endorsed by the Medical Associations and the Association of Statutory Health Insurance Physicians of the Federal States of Lower Saxony, Schleswig-Holstein and Hamburg.

RESULTS

A total of 858 incident cases and 1,821 population controls were included in this analysis. Table I shows the distribution of selected characteristics among cases and controls. The matched study design resulted in balance between cases and controls with respect to age and sex. The average age of NHL_{high} cases (54.9 years) was lower than the average age of NHL_{low} cases (57.3 years), while the average age of CLL cases (59.6 years) was higher than that of NHL_{low} cases. For each NHL subtype, the percentage of controls in the lowest quintile of socioeconomic status was less than the percentage among cases. For NHL_{low} and NHL_{high} the percentage of controls in the highest quintile was higher than among cases, while for CLL cases and controls appear relatively well balanced with respect to the other quintiles of this composite index of socioeconomic status. When considering cigarette smoking, the percentages of current smokers among CLL cases was greater than percentages among controls. The opposite pattern is observed for NHL_{low} and NHL_{high}.

Table I also shows the distribution of cases and controls by longest-held occupation, defined in terms of major occupational categories (i.e., one-digit ISCO-68 codes). When considering NHL_{high} and NHL_{low}, the percentages of cases employed in professional, administrative, and clerical occupations was less than the percentages of controls. The percentage of NHL_{high} cases employed in agricultural occupations was more than twice the percentage of controls. The percentage of NHL_{low} cases employed in agricultural occupations also was greater than the percentage of controls. CLL cases and controls were very comparable when examined by major occupational categories.

Odds ratios were calculated with respect to longest-held occupation, defined by minor occupational categories (i.e., two-digit ISCO-68 codes, Appendix Table A1 available with electronic version of the paper). Among the occupational categories in which at least five cases of NHL_{high} were observed, notably elevated odds ratios were observed for farmers [odds ratio (OR) = 1.98, 95% confidence interval

TABLE I. Distribution of Cases and Controls by Sub-Type of Lymphoma With Respect to Attained Age, Sex, Socioeconomic Status, Smoking Status, and Longest-Held Occupation, Northern Germany, 1986–1998

	NHL_{high}		NHL_{low}		CLL	
Characteristic	**Cases, n (%)**	**Controls, n (%)**	**Cases, n (%)**	**Controls, n (%)**	**Cases, n (%)**	**Controls, n (%)**
Sex						
Male	156 (64)	344 (66)	214 (56)	473 (58)	159 (68)	332 (69)
Female	86 (36)	181 (34)	167 (44)	343 (42)	76 (32)	148 (31)
Socioeconomic status						
Low	28 (12)	30 (6)	38 (10)	44 (5)	30 (13)	25 (5)
Medium–low	50 (21)	46 (9)	71 (19)	92 (11)	30 (13)	61 (13)
Medium	72 (30)	164 (31)	114 (30)	255 (31)	75 (32)	165 (34)
Medium–high	42 (17)	112 (21)	63 (17)	163 (20)	30 (13)	85 (18)
High	50 (21)	173 (33)	95 (25)	262 (32)	70 (30)	144 (30)
Smoking status						
Never smoked	114 (47)	218 (42)	173 (45)	334 (41)	104 (44)	204 (43)
Ex-smoker	70 (29)	173 (33)	113 (30)	262 (32)	71 (30)	172 (36)
Current smoker	58 (24)	134 (25)	95 (25)	220 (27)	60 (26)	104 (22)
Occupation major group [ISCO-68 Code]						
Professional, technical, and related [0/1]	23 (10)	93 (18)	45 (12)	143 (18)	31 (13)	87 (18)
Administrative and managerial [2]	4 (2)	19 (4)	10 (3)	33 (4)	12 (5)	18 (4)
Clerical and related [3]	28 (12)	102 (19)	55 (14)	148 (18)	37 (16)	81 (17)
Sales [4]	23 (10)	34 (6)	42 (11)	68 (8)	16 (7)	38 (8)
Service [5]	15 (6)	23 (4)	22 (6)	49 (6)	10 (4)	21 (4)
Agriculture, forestry, and fishermen [6]	26 (11)	25 (5)	29 (8)	38 (5)	15 (6)	30 (6)
Production, transport operators and laborers [7/8/9]	68 (28)	130 (25)	94 (25)	166(20)	62 (26)	136 (28)
Not classifiable (e.g., not in labor force)	55 (23)	99 (19)	84 (22)	171 (21)	52 (22)	69 (14)
Total number of observations	242	525	381	816	235	480
Age, in years [mean (SD)]	54.9 (13)	53.7 (14)	57.3 (10)	56.2 (11)	59.6 (9)	59.5 (10)

NHL_{high}, high-malignancy non-Hodgkin's lymphoma; NHL_{low}, low-malignancy non-Hodgkin's lymphoma; CLL, chronic lymphocytic leukemia.

(CI): 0.98, 3.98] and agricultural workers and husbandry workers (OR = 2.67, 95% CI: 0.99, 7.21). Elevations of NHL_{low} risk were observed among agricultural workers and husbandry workers (OR = 2.46, 95% CI: 1.17, 5.16), blacksmiths, toolmakers, and machine tool operators (OR = 3.12, 95% CI: 1.31, 7.47), and laborers not elsewhere classified (OR = 4.92, 95% CI: 0.95, 25.46). Building caretaker and cleaners exhibited elevated risks of NHL_{high} and NHL_{low} (OR = 2.04 and 2.43, respectively), as did technical salesmen, commercial travelers and manufacturers' agents (OR = 1.81 and 1.67, respectively), and salesmen, shop assistants, and related workers (OR = 1.25 and 1.09, respectively). Bricklayers, carpenters, and other construction workers also exhibited elevated risks of NHL_{high} and NHL_{low} (OR = 1.22 and 1.74, respectively). Among the occupational categories in which at least five CLL cases were observed, notably elevated risks were observed among electrical fitters and related electrical and electronic workers (OR = 2.52, 95% CI: 0.95, 6.64) and clerical and related workers (OR = 2.13, 95% CI: 0.90, 5.06).

Table II shows estimated odds ratios in relation to estimated exposure (ever vs. never potentially exposed) to 50 occupational agents. Potential exposure to arsenic compounds was associated with elevated risks of NHL_{high} (OR = 1.94, 95% CI: 1.34, 2.80) and NHL_{low} (OR = 1.33, 95% CI: 1.00, 1.78). Potential exposure to chlorophenols was associated with elevated odds of NHL_{high} (OR = 1.95, 95% CI: 1.32, 2.87) and NHL_{low} (OR = 1.32, 95% CI: 0.95, 1.82). Elevated odds ratios for NHL_{high} and NHL_{low} were also observed for occupational exposure potential to cold (OR = 1.53 and 1.34, respectively), diesel fuel (OR = 1.54 and 1.46, respectively), herbicides (OR = 2.17 and 1.37, respectively), and nitrates, nitrites, nitrosamines (OR = 2.22 and 1.45, respectively). Organic dust exposure was associated with elevated risks of NHL_{high} (OR = 2.29, 95% CI: 1.54, 3.38) and NHL_{low} (OR = 1.53, 95% CI: 1.12, 2.08),

TABLE II. Estimated Odds Ratios (and Associated 95% Confidence Intervals) for High-Malignancy Non-Hodgkin's Lymphoma, Low-Malignancy Non-Hodgkin's Lymphoma, and Chronic Lymphocytic Leukemia According to Ever Versus Never Exposure to Selected Occupational Agents, Northern Germany, 1986–1998

	NHL_{high}		NHL_{low}		CLL	
Agent	**No. exposed cases**	**OR (95% CI)[a]**	**No. exposed cases**	**OR (95% CI)[a]**	**No. exposed cases**	**OR (95% CI)[a]**
Acrylonitrile	4	1.15 (0.34, 3.86)	8	1.03 (0.43, 2.47)	4	0.99 (0.30, 3.32)
Active	119	1.11 (0.81, 1.51)	214	1.18 (0.92, 1.51)	128	1.14 (0.83, 1.57)
Adhesives-natural	75	1.04 (0.75, 1.43)	124	1.00 (0.76, 1.30)	82	1.21 (0.86, 1.68)
Adhesives-synthetic	112	1.01 (0.75, 1.37)	178	1.01 (0.79, 1.30)	124	1.29 (0.94, 1.76)
Antiknock agents	31	1.03 (0.63, 1.67)	56	1.45 (1.00, 2.11)	29	0.96 (0.60, 1.55)
Aromatic amines	29	0.96 (0.60, 1.53)	72	1.43 (1.03, 1.99)	30	0.68 (0.42, 1.10)
Arsenic and compounds	70	1.94 (1.34, 2.80)	108	1.33 (1.00, 1.78)	58	1.01 (0.70, 1.46)
Asbestos	72	1.26 (0.87, 1.84)	110	1.59 (1.15, 2.19)	66	0.80 (0.55, 1.17)
Benzene	48	1.13 (0.77, 1.68)	93	1.28 (0.95, 1.74)	47	0.76 (0.51, 1.14)
Beryllium and compounds	7	0.46 (0.20, 1.06)	7	0.55 (0.24, 1.27)	12	1.24 (0.58, 2.64)
Cadmium and compounds	32	0.90 (0.57, 1.43)	47	1.08 (0.74, 1.57)	32	1.20 (0.73, 1.97)
Carbon tetrachloride	50	1.12 (0.75, 1.66)	98	1.31 (0.97, 1.77)	50	0.74 (0.50, 1.08)
Chlorophenols	61	1.95 (1.32, 2.87)	77	1.32 (0.95, 1.82)	44	0.88 (0.59, 1.31)
Chromium/chromates	53	1.05 (0.72, 1.54)	108	1.44 (1.08, 1.92)	73	1.08 (0.76, 1.54)
Cold	82	1.53 (1.08, 2.16)	127	1.34 (1.02, 1.76)	80	1.13 (0.81, 1.57)
Contact-animals	65	1.81 (1.24, 2.66)	82	1.06 (0.78, 1.45)	46	0.85 (0.58, 1.24)
E.M. Fields	21	0.59 (0.34, 0.99)	33	1.04 (0.67, 1.61)	31	1.07 (0.66, 1.72)
Contact-public	109	0.98 (0.70, 1.36)	207	1.17 (0.90, 1.52)	109	0.95 (0.68, 1.33)
Cutting oils	9	0.80 (0.36, 1.78)	32	1.91 (1.17, 3.14)	11	0.83 (0.39, 1.77)
Degreasing agents	49	1.38 (0.93, 2.06)	81	1.28 (0.93, 1.76)	46	0.88 (0.59, 1.31)
Detergents	46	1.00 (0.67, 1.49)	98	1.19 (0.89, 1.60)	54	1.12 (0.77, 1.64)
Diesel fuel	90	1.54 (1.09, 2.17)	139	1.46 (1.12, 1.92)	79	0.95 (0.68, 1.35)
Dyestuffs	18	1.12 (0.62, 2.02)	39	1.14 (0.75, 1.72)	15	0.86 (0.46, 1.61)
Dust-cereals	53	1.69 (1.13, 2.53)	70	1.23 (0.87, 1.73)	48	1.16 (0.78, 1.72)
Dust-coal	8	0.74 (0.33, 1.67)	18	1.36 (0.73, 2.54)	13	0.91 (0.45, 1.83)
Dust-inorganic	39	1.43 (0.92, 2.22)	61	1.46 (1.01, 2.10)	39	1.02 (0.65, 1.60)
Dust-organic	61	2.29 (1.54, 3.38)	97	1.53 (1.12, 2.08)	46	1.02 (0.68, 1.51)
Dust-textiles	19	1.75 (0.91, 3.35)	24	1.04 (0.61, 1.76)	10	0.46 (0.22, 0.96)
Dust-wood	15	0.92 (0.49, 1.72)	25	1.14 (0.68, 1.91)	21	1.13 (0.64, 1.99)
Epoxy resins	40	0.89 (0.58, 1.35)	61	1.19 (0.83, 1.70)	44	1.03 (0.68, 1.55)
Ethylene oxide	6	0.57 (0.23, 1.44)	14	0.83 (0.43, 1.60)	6	0.80 (0.30, 2.14)
Formaldehyde	27	1.52 (0.88, 2.63)	45	1.18 (0.79, 1.75)	29	1.16 (0.71, 1.89)
Heat	24	0.66 (0.40, 1.08)	52	0.95 (0.66, 1.37)	34	1.02 (0.63, 1.65)
P.A.H's	58	1.17 (0.80, 1.70)	108	1.48 (1.10, 1.99)	57	0.88 (0.61, 1.27)
Herbicides	56	2.17 (1.44, 3.25)	79	1.37 (0.99, 1.90)	43	1.15 (0.76, 1.74)
Ionising radiation	6	0.31 (0.13, 0.75)	24	0.93 (0.56, 1.54)	5	0.38 (0.14, 0.99)
Lead and lead compounds	61	1.01 (0.69, 1.46)	102	1.18 (0.88, 1.58)	63	1.04 (0.71, 1.52)
Mercury and compounds	23	0.68 (0.42, 1.13)	46	1.03 (0.70, 1.51)	29	1.25 (0.76, 2.04)
Nitrate, nitrite, nitrosamine	56	2.22 (1.48, 3.35)	81	1.45 (1.05, 2.01)	40	1.07 (0.70, 1.63)
Organic solvents	62	0.92 (0.64, 1.32)	108	1.16 (0.87, 1.55)	70	0.96 (0.67, 1.36)
Outdoor occupation	85	1.27 (0.92, 1.76)	147	1.33 (1.02, 1.72)	89	1.09 (0.78, 1.51)
Paints and pigments	46	1.01 (0.67, 1.53)	81	1.62 (1.15, 2.29)	54	0.98 (0.67, 1.43)
Polychlorinated biphenyl	55	0.82 (0.57, 1.17)	94	0.95 (0.72, 1.26)	66	1.48 (1.02, 2.15)
Printing inks	42	0.97 (0.64, 1.45)	72	0.98 (0.71, 1.35)	47	1.89 (1.21, 2.96)
Solder fumes	42	0.84 (0.55, 1.31)	59	0.99 (0.69, 1.42)	45	1.04 (0.69, 1.57)
Soot, tar, mineral oil	72	1.13 (0.79, 1.62)	119	1.33 (1.00, 1.77)	65	0.95 (0.66, 1.35)
Styrene	36	1.47 (0.92, 2.32)	54	1.30 (0.89, 1.91)	31	0.94 (0.58, 1.54)
Ultraviolet light	18	0.68 (0.39, 1.18)	45	1.00 (0.68, 1.47)	34	1.66 (1.00, 2.74)
Waxes and polishes	47	1.32 (0.87, 2.00)	99	1.28 (0.95, 1.72)	58	1.27 (0.86, 1.88)
Welding fumes	37	1.26 (0.80, 1.97)	61	1.37 (0.95, 1.98)	33	0.90 (0.58, 1.40)

NHL_{high}, high-malignancy non-Hodgkin's lymphoma; NHL_{low}, low-malignancy non-Hodgkin's lymphoma; CLL, chronic lymphocytic leukemia.
[a]Estimated odds ratio, OR, derived from a conditional logistic regression model with adjustment for a three-level indicator of smoking status and 95% Wald confidence interval (95% CI). People never exposed to the agent constituted the reference group.

as was exposure to cereal dust (OR = 1.69 and 1.23, respectively) and inorganic dust (OR = 1.43 and 1.46, respectively).

Occupations involving contact with animals were associated with elevated odds of NHL_{high} (OR = 1.81, 95% CI: 1.24, 2.66) but not NHL_{low} or CLL. Low-malignancy NHL was associated with potential exposure to antiknock agents (OR = 1.45), aromatic amines (OR = 1.43), asbestos (OR = 1.59), chromium and chromates (OR = 1.44), cutting oils (OR = 1.91), PAH's (OR-1.48), paints and pigments (OR = 1.62), and soot, tar, and mineral oil (OR = 1.33), while these agents exhibited little or no association with NHL_{high} and CLL. CLL exhibited elevated odds ratios for potential exposure to polychlorinated biphenyl (OR = 1.48, 95% CI: 1.02, 2.15), printing inks (OR = 1.89, 95% CI: 1.21, 2.96), and ultraviolet light (OR = 1.66, 95% CI: 1.00, 2.74). Workers who were ever employed in jobs judged to involve potential occupational exposure to ionizing radiation were at lower risk of CLL and NHL_{high} (OR = 0.38 and 0.31, respectively).

Table III presents the results of investigations of associations in relation to cumulative exposure to 15 selected agents. We calculated odds ratios for categories of cumulative exposure defined by tertiles of the cumulative exposure distribution among exposed controls, with the reference category being those who were estimated to have no exposure to the agent under study. The only monotonic trend in odds ratios across categories defined by tertiles of cumulative exposure to an agent was observed between NHL_{low} and diesel fuel (*P*-value = 0.03). However, for several of exposure-disease associations the most highly-elevated odds ratio estimates were obtained for workers in the highest tertile of estimated cumulative exposure. This includes associations between arsenic compounds and NHL_{high} (odds ratio for highest tertile vs. never exposed = 2.31, 95% CI: 1.33, 4.01), arsenic compounds and NHL_{low} (odds ratio for highest tertile vs. never exposed = 1.43, 95% CI: 0.93, 2.22), chlorophenols and NHL_{low} (odds ratio for highest tertile vs. never exposed = 1.70, 95% CI: 1.03, 2.81), chromium/chromates and NHL_{high} (odds ratio for highest tertile vs. never exposed = 2.25, 95% CI: 1.23, 4.10), diesel fuel and NHL_{low} (odds ratio for highest tertile vs. never exposed = 1.55, 95% CI: 1.04, 2.32), herbicides and NHL_{low} (odds ratio for highest tertile vs. never exposed = 1.64, 95% CI: 0.96, 2.80), soot, tar, mineral oil, and NHL_{low} (odds ratio for highest tertile vs. never exposed = 1.85, 95% CI: 1.23, 2.77), and printing inks and CLL (odds ratio for highest tertile vs. never exposed = 2.40, 95% CI: 1.25, 4.61).

DISCUSSION

In this study we examined associations between occupational factors and NHL risk. When we classified study members by longest-held occupation, we noted evidence of elevated risk of NHL_{high} and/or NHL_{low} among farmers and agricultural workers, workers involved in machine tool operation, construction workers, and people employed in a variety of sales occupations. These findings are interesting to contrast to findings of a recent report by Mester et al. [2006], which examined the association between occupation and lymphoma risk among people in a different region of Germany. Similar to this study, Mester et al. found that people employed as farmers were at increased risk of lymphoma (OR = 2.4, 95% CI: 1.1, 5.4), as were carpenters, bricklayers and other construction workers (OR = 1.7, 95% CI: 1.0, 2.8). Architects and maids, two occupational groups that were noted by Mester et al. to be at significantly increased risk of lymphoma were not found to be at significantly elevated risk of NHL in our study.

We used detailed occupational history information in conjunction with a previously-developed JEM in order to derive estimates of occupational exposure to a variety of agents. Some studies have suggested a relationship between electromagnetic field exposures and NHL [Villeneuve et al., 2000]; in this study we observed a deficit of cases of NHL_{high} among those with estimated potential exposure to EMF. Combined studies suggest a small excess of lymphoma risk among those exposed to asbestos [Becker et al., 2001]. We observed evidence of positive associations between NHL (NHL_{high} and NHL_{low}) and potential exposure to asbestos and to inorganic dust. In our analyses, estimated exposure potential to organic dust exhibited stronger associations with NHL than did asbestos.

Herbicide and pesticide exposures have been of major interest in relation to NHL risk, in part because of the consistent evidence of increased NHL risk among farmers and agricultural workers [Blair et al., 1998; Schroeder et al., 2001; Zheng et al., 2001; De Roos et al., 2003; Hartge et al., 2006; Boffetta and de Vocht, 2007]. Our study found elevated risks of NHL_{high} and NHL_{low} among agricultural workers, and elevated risk of NHL_{high} and NHL_{low} among those with estimated herbicide exposure potential. We observed a positive association between NHL_{high} risk and estimated exposure potential to chlorophenols (ever vs. never), exposure potential to herbicides, and exposure potential to arsenic compounds. The main occupations held by persons who were classified as potentially exposed to herbicides were "farmers (farmers owning their own farm, or helper on the farm)" and gardeners working in horticulture or tree nurseries. The latter occupations were important because there are a large number of tree nurseries and horticultural companies located in the study area. These same occupations were the leading jobs held by persons who were classified as potentially exposed to arsenic and arsenic compounds; other jobs that were less common, but also judged to have potential exposure to arsenic were blacksmiths, fitters, and metalworkers.

TABLE III. Estimated Odds Ratios (and Associated 95% Confidence Intervals) for High-Malignancy Non-Hodgkin's Lymphoma, Low-Malignancy Non-Hodgkin's Lymphoma, and Chronic Lymphocytic Leukemia According to Estimates of Cumulative Exposure to Selected Occupational Agents, Northern Germany, 1986–1998

	NHL_{high} (n = 242)		NHL_{low} (n = 381)		CLL (n = 235)	
	Cases	OR (95% CI)[a]	Cases	OR (95% CI)[a]	Cases	OR (95% CI)[a]
Arsenic and compounds						
Cumulative exposure[b]						
>0–11,279	20	1.81 (0.98, 3.33)	36	1.39 (0.89, 2.17)	15	0.88 (0.47, 1.63)
11,280–38,915	20	1.56 (0.85, 2.86)	35	1.25 (0.79, 1.98)	26	1.48 (0.85, 2.58)
38,916–197,870	30	2.31 (1.33, 4.01)	37	1.43 (0.93, 2.22)	17	0.81 (0.45, 1.46)
Linear trend		$P = 0.003$		$P = 0.045$		$P = 0.833$
Asbestos						
Cumulative exposure[b]						
>0–20,303	16	0.77 (0.41, 1.43)	39	1.80 (1.13, 2.85)	23	0.99 (0.57, 1.72)
20,304–60,488	25	1.67 (0.94, 2.97)	28	1.26 (0.76, 2.08)	15	0.44 (0.23, 0.83)
60,489–397,197	30	1.43 (0.83, 2.45)	43	1.81 (1.16, 2.81)	28	1.08 (0.64, 1.81)
Linear trend		$P = 0.091$		$P = 0.028$		$P = 0.821$
Chlorophenols						
Cumulative exposure[b]						
>0–12,924	24	2.79 (1.52, 5.09)	27	1.24 (0.75, 2.07)	12	0.87 (0.43, 1.75)
12,925–40,607	13	1.19 (0.58, 2.44)	20	1.05 (0.59, 1.88)	15	0.91 (0.48, 1.75)
40,608–197,870	24	1.86 (1.04, 3.33)	30	1.70 (1.03, 2.81)	17	0.88 (0.49, 1.60)
Linear trend		$P = 0.068$		$P = 0.068$		$P = 0.770$
Chromium/chromates						
Cumulative exposure[b]						
>0–15,791	12	0.70 (0.36, 1.36)	37	1.55 (0.99, 2.40)	25	1.16 (0.69, 1.93)
15,792–51,511	13	0.63 (0.32, 1.23)	37	1.57 (1.00, 2.46)	27	1.29 (0.77, 2.17)
51,512–387,750	28	2.25 (1.23, 4.10)	34	1.29 (0.80, 2.08)	21	0.81 (0.46, 1.44)
Linear trend		$P = 0.028$		$P = 0.054$		$P = 0.443$
Contact-animals						
Cumulative exposure[b]						
>0–49,349	18	1.55 (0.84, 2.86)	23	0.93 (0.56, 1.54)	7	0.43 (0.19, 1.01)
49,350–228,419	21	2.40 (1.23, 4.70)	26	0.96 (0.58, 1.57)	21	1.19 (0.68, 2.08)
228,420–1,780,830	26	1.79 (1.03, 3.12)	33	1.33 (0.85, 2.11)	18	0.89 (0.50, 1.58)
Linear trend		$P = 0.042$		$P = 0.115$		$P = 0.847$
Diesel fuel						
Cumulative exposure[b]						
>0–25,379	31	1.87 (1.12, 3.12)	52	1.45 (0.99, 2.13)	27	1.02 (0.61, 1.70)
25,380–92,119	26	1.24 (0.74, 2.10)	40	1.47 (0.96, 2.25)	27	0.97 (0.58, 1.61)
92,120–432,870	33	1.68 (1.00, 2.82)	47	1.55 (1.04, 2.32)	24	0.83 (0.49, 1.42)
Linear trend		$P = 0.019$		$P = 0.032$		$P = 0.828$
Dust-inorganic						
Cumulative exposure[b]						
>0–20,303	7	0.68 (0.29, 1.61)	19	1.47 (0.79, 2.72)	14	1.94 (0.87, 4.34)
20,304–88,829	21	2.96 (1.50, 5.83)	22	1.34 (0.76, 2.36)	7	0.45 (0.17, 1.14)
88,830–448,944	11	1.21 (0.56, 2.62)	20	1.82 (0.97, 3.41)	18	1.07 (0.58, 1.97)
Linear trend		$P = 0.194$		$P = 0.054$		$P = 0.518$

(*Continued*)

TABLE III. (*Continued*)

	NHL_{high} (n = 242)		NHL_{low} (n = 381)		CLL (n = 235)	
	Cases	OR (95% CI)[a]	Cases	OR (95% CI)[a]	Cases	OR (95% CI)[a]
Dust-organic						
Cumulative exposure[b]						
>0–13,535	19	2.91 (1.48, 5.74)	37	1.52 (0.97, 2.40)	14	1.07 (0.55, 2.09)
13,536–50,759	14	1.60 (0.78, 3.29)	31	1.45 (0.88, 2.38)	15	1.02 (0.54, 1.95)
50,760–592,200	28	2.43 (1.36, 4.33)	29	1.61 (0.98, 2.65)	17	0.99 (0.54, 1.82)
Linear trend		$P = 0.002$		$P = 0.156$		$P = 0.965$
Herbicides						
Cumulative exposure[b]						
>0–17,154	17	1.81 (0.94, 3.48)	26	1.33 (0.79, 2.24)	13	1.34 (0.66, 2.73)
17,155–122,199	16	2.94 (1.37, 6.33)	27	1.21 (0.73, 2.01)	15	1.27 (0.65, 2.48)
122,200–526,870	23	2.08 (1.15, 3.77)	26	1.64 (0.96, 2.80)	15	1.00 (0.53, 1.89)
Linear trend		$P = 0.024$		$P = 0.051$		$P = 0.755$
Nitrate, nitrite, nitrosamine						
Cumulative exposure[b]						
>0–26,084	22	3.13 (1.64, 5.97)	31	1.47 (0.91, 2.40)	9	0.97 (0.42, 2.20)
26,085–112,799	11	1.19 (0.55, 2.59)	22	1.26 (0.72, 2.21)	17	1.44 (0.76, 2.72)
112,800–593,610	23	2.39 (1.29, 4.42)	28	1.65 (0.99, 2.74)	14	0.91 (0.47, 1.73)
Linear trend		$P = 0.031$		$P = 0.046$		$P = 0.884$
Polychlorinated biphenyl						
Cumulative exposure[b]						
>0–11,279	16	0.78 (0.43, 1.41)	32	0.95 (0.61, 1.47)	16	1.34 (0.70, 2.55)
11,280–32,147	16	0.68 (0.38, 1.21)	31	0.99 (0.64, 1.55)	22	1.45 (0.82, 2.56)
32,148–269,028	20	0.91 (0.52, 1.60)	31	0.96 (0.61, 1.50)	28	1.60 (0.94, 2.72)
Linear trend		$P = 0.406$		$P = 0.498$		$P = 0.215$
Printing inks						
Cumulative exposure[b]						
>0–12,304	16	1.19 (0.62, 2.29)	23	0.97 (0.57, 1.65)	13	1.66 (0.78, 3.55)
12,305–32,922	9	0.64 (0.30, 1.37)	24	1.01 (0.60, 1.71)	13	1.46 (0.71, 2.99)
32,923–928,485	14	0.91 (0.47, 1.75)	25	1.01 (0.62, 1.65)	21	2.40 (1.25, 4.61)
Linear trend		$P = 0.878$		$P = 0.888$		$P = 0.102$
Soot, tar, mineral oil						
Cumulative exposure[b]						
>0–30,737	19	1.01 (0.57, 1.80)	29	0.85 (0.53, 1.36)	15	0.70 (0.37, 1.31)
30,738–110,402	29	1.28 (0.76, 2.16)	37	1.51 (0.97, 2.34)	25	0.99 (0.58, 1.68)
110,403–1,191,591	23	1.06 (0.61, 1.83)	53	1.85 (1.23, 2.77)	24	1.05 (0.62, 1.77)
Linear trend		$P = 0.239$		$P = 0.063$		$P = 0.611$

NHL_{high}, high-malignancy non-Hodgkin's lymphoma; NHL_{low}, low-malignancy non-Hodgkin's lymphoma; CLL, chronic lymphocytic leukemia.
[a]Estimated odds ratio, OR, derived from a conditional logistic regression model with adjustment for a three-level indicator of smoking status and 95% Wald confidence interval (95% CI). People never exposed to the agent constituted the reference group.
[b]Defined as the product of cumulative hours worked in each exposed job, and the respective exposure intensity and probability scores.

Benzene, a well-established leukemogen, has not been shown to be strongly associated with NHL, although some studies have suggested an association [Hayes et al., 1997; Savitz and Andrews, 1997; Smith et al., 2007]. In our analyses, we did not observe strong evidence of association between NHL risk and estimated benzene exposure; odds ratios for NHL_{high} and NHL_{low} were greater than unity for workers with estimated exposure to benzene but estimated associations were highly imprecise. Mineral oil has been suggested as a cause of lymphatic cancer [Hours et al., 1995; Mao et al., 2000]. In our analyses there was evidence of a positive association between estimated cumulative exposure to soot, tar and mineral oil and NHL; this association was primarily due to elevated NHL risk amongst workers in the highest tertile of exposure. Jobs that involved plausible exposures to zoonotic infections have been of interest in

relation to NHL. In our analyses, jobs estimated to involve contact with animals were associated with elevated risks of NHL_{high} (OR = 1.81, 95% CI: 1.24, 2.66) but not NHL_{low} or CLL.

We found relatively little impact of varying exposure lag assumptions between 2 and 10 years on the risk estimates derived from cumulative exposure-NHL associations (results not shown). The consistency of the findings under 2- and 10-year lag assumptions suggests that the associations between occupational exposures and NHL risk that we have observed are due primarily to associations with cumulative exposures accrued in the period 10 or more years in the past; recently accrued exposures (i.e., those that occurred in the period 2–10 years prior to diagnosis) exhibited little association with NHL risk. This pattern is noteworthy in that it differs from the temporal patterns of risk observed in analyses, for example, of relationships between benzene exposure and leukemia (where a prompt peak in excess risk is observed that diminishes with continued time since exposure [Silver et al., 2002]). However, for diseases that progress slowly, particularly lymphatic malignancies such as CLL, a protracted latent period between exposure and clinically overt disease is plausible.

For most of the analyses in which we examined associations between cumulative exposure to an agent and disease risk we failed to observe a monotonic trend in odds ratios across categories defined by tertiles of cumulative exposure (Table III); in many instances, small *P* values were derived for tests of linear cumulative exposure-disease associations although examination of category-specific odds ratios suggested that the distinction of primary importance was between people who were not judged to have potential for exposure to the agent and those who had any potential exposure to the agent. That said, for a number of the occupational agents the odds ratio of greatest magnitude and precision was derived for workers in the highest tertile of estimated cumulative exposure. This includes associations between arsenic compounds and NHL_{high}, arsenic compounds and NHL_{low}, chlorophenols and NHL_{low}, chromium/chromates and NHL_{high}, diesel fuel and NHL_{low}, herbicides and NHL_{low}, soot, tar, mineral oil and NHL_{low}, and printing inks and CLL.

The diagnostic category of NHL encompasses a heterogeneous group of malignant lymphatic diseases. Over the last two decades there have been a number of attempts to divide the diagnostic category of NHL into subgroups of cases that appear to share biological, clinical, and behavioral commonalities. For the purposes of these analyses, NHL cases were divided into subgroups following the revised Kiel classification, which was state-of-the-art at the time of study initiation [Lennert and Feller, 1992]. While the Kiel classification refers to NHL of ‘‘low’’ versus ‘‘high’’ malignancy, the more recent revised European-American classification of lymphoid neoplasms refers to ‘‘low grade’’ versus ‘‘high grade’’ NHL [Harris et al., 1994] and the recent World Health Organization classification refers to ‘‘precursor’’ versus ‘‘mature’’ B- and T-neoplasms [Harris et al., 1999]. These three classifications yield differences in the grouping of certain lymphoma entities, although these differences are small in terms of numbers and the corresponding categories broadly overlap.

We have used detailed occupational history information in conjunction with a previously-developed JEM in order to derive quantitative occupational exposure estimates. There are certainly limitations to this form of occupational exposure assessment, particularly when contrasted with studies that utilize quantitative individual exposure measurement data; however, prior research has demonstrated that this type of JEM is useful for discriminating between groups of workers with different exposures. Even when using a single reported primary occupation during the lifetime, such as reported on the death certificate, classifications via this sort of JEM have been shown to identify subgroups of workers with plausible excesses of occupationally-related diseases [Coggon et al., 1984]. In our study, we had relatively detailed occupational exposure history information that permitted us to derive estimates of the numbers of hours worked in different occupations. Theoretical studies also provide some basis for confidence in the application of JEMs to occupational exposure assessments. To the extent that JEMs allow an investigator to discriminate between subgroups of workers in terms of average exposure rates, estimates of exposure-response trends tend to suffer a relatively small degree of bias even if the assumptions of Berkson error are violated to a moderate degree [Kim et al., 2006]. That said, questions about the accuracy and validity of the exposure assessments employed in these analyses are warranted; further analyses could be done to evaluate the consistency of results when exposure estimates were restricted to those with the highest certainty of exposure, and ideally some of the associations suggested by these analyses will be evaluated in studies that utilize quantitative individual exposure measurement data.

As is typical in population-based case–control studies, the possibility exists that socioeconomic differences in participation rates have led to a biased control sample. For example, it is plausible that controls of higher socioeconomic status may have agreed to participate in the study more often than controls of lower socioeconomic status. This may in part explain the higher percentage of controls in the upper socioeconomic status categories than cases in these socioeconomic categories. Since socioeconomic status is related to occupation, such biases could influence conclusions about the relationship between NHL risk and primary occupation; for example, we observed that administrators and professionals tended to be at lower risk of NHL than other occupations.

In conclusion, this study provides suggestive evidence of associations between NHL risk and occupational exposure to

a number of agents, including arsenic compounds, asbestos, chlorophenols, chromium, contact with animals, diesel fuel, organic and inorganic dusts, herbicides, nitrites/nitrates/ nitrosamines, and soot/tar/mineral oil. These associations were primarily with NHL_{high} and NHL_{low}, rather than with CLL. These findings provide further insights into potential occupational risk factors for NHL and suggest some specific occupational agents for further investigation.

ACKNOWLEDGMENTS

Dr. Richardson was supported by a fellowship from the Alfried Krupp Wissenschaftskolleg Greifswald funded by the Alfried Krupp von Bohlen und Halbach-Stiftung. The Northern Germany Leukaemia and Lymphoma Study (NLL) was funded by grants from the Ministry of Environment, Nature Protection and Agriculture, Schleswig-Holstein, and the Ministry of Social Affairs, Women, Family and Health, Lower Saxony. For cooperation during the study period we would like to thank the representatives of the ministries: Klaus-Dietrich Sturm (Kiel, Schleswig-Holstein) and Michael Csicsaky (Hannover, Lower Saxony). We are grateful to the all participants of the Northern Germany Leukaemia and Lymphoma Study (NLL) and all the physicians, who provided access to patients' files for the incidence study and helped to communicate the importance of participation in this study to their patients. We would also like to thank the members of the Scientific Advisory Board: Karl-Heinz Jöckel (Chairman, Essen), Ursula Ackermann-Liebrich (Co-Chairwomen, Basel, Switzerland), Jürgen Berger (Hamburg), Michael Schümann (Hamburg), Fred Stevenson[†] (Kiel), and Heinz-Erich Wichmann (Neuherberg), as well as the associated experts of the Advisory Board: Dietrich Harder (Göttingen), and Hermann Heimpel (Ulm).

REFERENCES

Becker N, Berger J, Bolm-Audorff U. 2001. Asbestos exposure and malignant lymphomas–a review of the epidemiological literature. Int Arch Occup Environ Health 74:459–469.

Blair A, Cantor KP, Zahm SH. 1998. Non-hodgkin's lymphoma and agricultural use of the insecticide lindane. Am J Ind Med 33:82–87.

Boffetta P, de Vocht F. 2007. Occupation and the risk of non-Hodgkin lymphoma. Cancer Epidemiol Biomarkers Prev 16:369–372.

Coggon D, Pannett B, Acheson ED. 1984. Use of job-exposure matrix in an occupational analysis of lung and bladder cancers on the basis of death certificates. J Natl Cancer Inst 72:61–65.

De Roos AJ, Zahm SH, Cantor KP, Weisenburger DD, Holmes FF, Burmeister LF, Blair A. 2003. Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men. Occup Environ Med 60:E11.

Dryver E, Brandt L, Kauppinen T, Olsson H. 2004. Occupational exposures and non-Hodgkin's lymphoma in Southern Sweden. Int J Occup Environ Health 10:13–21.

† Deceased in 2006.

Eurostat. 1990. NACE, rev. 1: Statistical classification of economic activities in the european community. Luxembourg: Eurostat.

Harris NL, Jaffe ES, Stein H, Banks PM, Chan JK, Cleary ML, Delsol G, De Wolf-Peeters C, Falini B, Gatter KC, Grogan TM, Isaacson PG, Knowles DM, Mason DY, Muller-Hermelink H, Pileri SA, Piris MA, Ralfkiaer E, Warnke RA. 1994. A revised European-American classification of lymphoid neoplasms: A proposal from the International Lymphoma Study Group. Blood 84:1361–1392.

Harris NL, Jaffe ES, Diebold J, Flandrin G, Muller-Hermelink HK, Vardiman J, Lister TA, Bloomfield CD. 1999. The World Health Organization classification of neoplastic diseases of the hematopoietic and lymphoid tissues. Report of the Clinical Advisory Committee meeting, Airlie House, Virginia, November, 1997. Ann Oncol 10:1419–1432.

Hartge P, Wang SS, Bracci PM, Devesa SS, Holly EA. 2006. Non-Hodgkin lymphoma. In: Schottenfeld D, Fraumeni JF, editors. Cancer epidemiology and prevention, 3rd edition. Oxford: Oxford University Press.

Hayes RB, Yin SN, Dosemeci M, Li GL, Wacholder S, Travis LB, Li CY, Rothman N, Hoover RN, Linet MS. 1997. Benzene and the dose-related incidence of hematologic neoplasms in China. Chinese Academy of Preventive Medicine–National Cancer Institute Benzene Study Group. J Natl Cancer Inst 89:1065–1071.

Hours M, Fevotte J, Ayzac L, Dananche B, Bergeret A, Milan JJ, Bonhomme I, Fiere D, Philippe J, Fabry J. 1995. Occupational exposure and malignant hemopathies: A case–control study in Lyon (France). Rev Epidemiol Sante Publique 43:231–241.

International Labor Organization. 1969. International standard classification of occupations, revised edition 1968. Geneva: ILO.

Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, Thun MJ. 2006. Cancer statistics, 2006. CA Cancer J Clin 56:106–130.

Kim HM, Yasui Y, Burstyn I. 2006. Attenuation in risk estimates in logistic and cox proportional-hazards models due to group-based exposure assessment strategy. Ann Occup Hyg 50:623–635.

Lennert K, Feller A. 1992. Histopathology of non-Hodgkin's lymphomas, 2nd edition. New York, NY: Springer-Verlag.

Mao Y, Hu J, Ugnat AM, White K. 2000. Non-Hodgkin's lymphoma and occupational exposure to chemicals in Canada. Canadian Cancer Registries Epidemiology Research Group. Ann Oncol 11:69–73.

Mester B, Nieters A, Deeg E, Elsner G, Becker N, Seidler A. 2006. Occupation and malignant lymphoma: A population based case control study in Germany. Occup Environ Med 63:17–26.

Morton LM, Hartge P, Holford TR, Holly EA, Chiu BC, Vineis P, Stagnaro E, Willett EV, Franceschi S, La Vecchia C, Hughes AM, Cozen W, Davis S, Severson RK, Bernstein L, Mayne ST, Dee FR, Cerhan JR, Zheng T. 2005. Cigarette smoking and risk of non-Hodgkin lymphoma: A pooled analysis from the International Lymphoma Epidemiology Consortium (interlymph). Cancer Epidemiol Biomarkers Prev 14:925–933.

Pannett B, Coggon D, Acheson ED. 1985. A job-exposure matrix for use in population based studies in England and Wales. Br J Ind Med 42:777–783.

Pearce N, Bethwaite P. 1992. Increasing incidence of non-Hodgkin's lymphoma: Occupational and environmental factors. Cancer Res 52:5496s–5500s.

SAS Institute, Inc. 2004. SAS OnlineDoc® 9.1.2. Cary, NC: SAS Institute Inc.

Savitz DA, Andrews KW. 1997. Review of epidemiologic evidence on benzene and lymphatic and hematopoietic cancers. Am J Ind Med 31:287–295.

Schroeder JC, Olshan AF, Baric R, Dent GA, Weinberg CR, Yount B, Cerhan JR, Lynch CF, Schuman LM, Tolbert PE, Rothman N, Cantor

KP, Blair A. 2001. Agricultural risk factors for t(14;18) subtypes of non-Hodgkin's lymphoma. Epidemiology 12:701–709.

Schroeder JC, Olshan AF, Baric R, Dent GA, Weinberg CR, Yount B, Cerhan JR, Lynch CF, Schuman LM, Tolbert PE, Rothman N, Cantor KP, Blair A. 2002. A case–control study of tobacco use and other non-occupational risk factors for t(14;18) subtypes of non-Hodgkin's lymphoma (United States). Cancer Causes Control 13:159–168.

Silver SR, Rinsky R, Cooper SP, Hornung RW, Lai D. 2002. Effect of follow-up time on risk estimates: A longitudinal examination of the relative risks of leukemia and multiple myeloma in a rubber hydrochlorine cohort. Am J Ind Med 42:481–489.

Smith MT, Jones RM, Smith AH. 2007. Benzene exposure and risk of non-Hodgkin lymphoma. Cancer Epidemiol Biomarkers Prev 16:385–391.

Villeneuve PJ, Agnew DA, Miller AB, Corey PN. 2000. Non-Hodgkin's lymphoma among electric utility workers in Ontario: The evaluation of alternate indices of exposure to 60 Hz electric and magnetic fields. Occup Environ Med 57:249–257.

Zahm SH, Weisenburger DD, Holmes FF, Cantor KP, Blair A. 1997. Tobacco and non-Hodgkin's lymphoma: Combined analysis of three case–control studies (United States). Cancer Causes Control 8:159–166.

Zheng T, Zahm SH, Cantor KP, Weisenburger DD, Zhang Y, Blair A. 2001. Agricultural exposure to carbamate pesticides and risk of non-Hodgkin lymphoma. J Occup Environ Med 43:641–649.

Zheng T, Blair A, Zhang Y, Weisenburger DD, Zahm SH. 2002. Occupation and risk of non-Hodgkin's lymphoma and chronic lymphocytic leukemia. J Occup Environ Med 44:469–474.

TABLE A1. Estimated Odds Ratios and Associated 95% Confidence Intervals for High-Malignancy Non-Hodgkin's Lymphoma, Low-Malignancy Non-Hodgkin's Lymphoma, and Chronic Lymphocytic Leukemia According to Longest-Held Occupation, Northern Germany, 1986–1998

	NHL_{high}		NHL_{low}		CLL	
Occupation group [ISCO-68 code]	**Cases**	**OR (95% CI)[a]**	**Cases**	**OR (95% CI)[a]**	**Cases**	**OR (95% CI)[a]**
Architects, Engineers and Related Technician [02]	5	0.48 (0.17, 1.348)	10	0.59 (0.29, 1.22)	9	0.96 (0.43 2.17)
Medical, Dental, Veterinary and Related Workers [07]	1	0.14 (0.02, 1.110)	5	0.90 (0.31, 2.67)	0	—
Teachers [13]	5	0.53 (0.20, 1.41)	12	0.78 (0.40, 1.52)	8	0.57 (0.25, 1.29)
Managers [21]	3	0.32 (0.09, 1.12)	9	0.57 (0.27, 1.20)	10	1.25 (0.54, 2.87)
Government Executive Officials [31]	13	0.49 (0.25, 0.93)	25	0.95 (0.58, 1.57)	11	0.46 (0.24,0.91)
Bookkeepers, Cashiers and Related [33]	7	0.70 (0.30, 1.63)	8	0.39 (0.18, 0.83)	9	1.17 (0.50, 2.76)
Clerical and Related Workers, n.e.c [39]	5	0.72 (0.25, 2.02)	18	1.28 (0.70, 2.35)	12	2.13 (0.90, 5.06)
Working Proprietors (Wholesale and Retail Trade) [41]	4	8.95 (0.99, 80.68)	1	0.50 (0.06, 4.52)	5	1.66 (0.50, 5.59)
Technical Salesmen, Commercial Travellers and Manufacturers' Agents [43]	5	1.81 (0.54, 6.08)	12	1.67 (0.77, 3.60)	4	1.78 (0.47, 6.73)
Salesmen, Shop Assistants and Related [45]	11	1.25 (0.58, 2.70)	20	1.09 (0.62, 1.93)	3	0.31 (0.09, 1.05)
Building Caretakers, Charworkers, Cleaners [55]	3	2.04 (0.40, 10.36)	9	2.43 (0.93, 6.35)	3	0.72 (0.19, 2.75)
Farmers [61]	17	1.98 (0.98, 3.98)	12	1.07 (0.53, 2.16)	7	0.88 (0.35, 2.20)
Agricultural Workers and Animal Husbandry Workers [62]	9	2.67 (0.99, 7.21)	16	2.46 (1.17, 5.16)	8	1.24 (0.51, 2.98)
Production Supervisors and General Foremen [70]	4	0.92 (0.28, 3.02)	6	1.24 (0.45, 3.36)	4	1.00 (0.30, 3.33)
Food and Beverage Processers [77]	3	0.69 (0.17, 2.70)	2	0.52 (0.11, 2.45)	5	2.35 (0.61, 9.12)
Blacksmiths, Toolmakers and Machine-Tool Operators [83]	5	1.20 (0.39, 3.75)	12	3.12 (1.31, 7.47)	2	0.44 (0.10, 2.05)
Machinery Fitters, Machine Assemblers and Precision Instrument Makers (except Electrical) [84]	10	1.01 (0.47, 2.17)	15	1.18 (0.62, 2.26)	9	1.03 (0.46, 2.34)
Electrical Fitters and Related Electrical and Electronics Workers [85]	5	0.75 (0.26, 2.13)	4	1.31 (0.38, 4.54)	9	2.52 (0.95, 6.64)
Plumbers, Welders, Sheet Metal and Structural Metal Preparers and Erectors [87]	5	2.34 (0.61, 8.94)	5	0.88 (0.30, 2.57)	0	—
Bricklayers, Carpenters and Other Construction Workers [95]	11	1.22 (0.57, 2.62)	16	1.74 (0.87, 3.50)	11	1.04 (0.48, 2.27)
Material-Handling and Related Equipment Operators, Dockers and Freight Handlers [97]	2	0.97 (0.19, 5.05)	6	1.26 (0.46, 3.49)	4	1.39 (0.37, 5.17)
Transport Equipment Operators [98]	8	0.96 (0.41, 2.26)	9	0.96 (0.42, 2.19)	6	0.85 (0.32, 2.24)
Labourers, n.e.c. [99]	0	—	5	4.92 (0.95, 25.46)	1	0.44 (0.05, 3.77)

Results shown for occupation groups in which at least five cases of NHL_{high}, NHL_{low}, or CLL were observed.
NHL_{high}, high-malignancy non-Hodgkin's lymphoma; NHL_{low}, low-malignancy non-Hodgkin's lymphoma; CLL, chronic lymphocytic leukemia.
[a]Estimated odds ratio, OR, derived from a conditional logistic regression model with adjustment for a three-level indicator of smoking status and 95% Wald confidence interval (95% CI).